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Review

Retrospective analysis of anesthetic management in the intracranial masses

Intracranial masses and anesthetic management

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Abstract

Aim: The aim of this study was to perform a retrospective review of the intracranial mass cases in our hospital and to investigate the effects of anesthesia management on these patients.

Material and Methods: The study universe of this study comprised patients who were given general anesthesia for intracranial mass surgery in the Anesthesiology and Reanimation Clinic of Ankara Numune Training and Research Hospital from 2008 to 2015.

Results: A review of the patient records in our hospital showed the data of 400 patients, who were older than 18 years and who were operated in our hospital for an intracranial mass.

Discussion: The current role of anesthesiologists has already passed beyond the line of ensuring the safety of the patient only during the operation but they aim to make critical contributions in the postoperative period as well.

Keywords

Intracranial mass; Anesthesiology; Peroperative management

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Introduction

During the intracranial mass excision surgery, the anesthetist is expected to maintain optimum conditions for the patient and surgeon perioperatively, maintaining cerebral perfusion appropriately, preventing brain edema and increases in the intracranial pressure, ensuring hemodynamic stability and fast and convenient recovery with early neurologic evaluation. The anesthetic agents given to the patient should allow for maintaining hemodynamic stability during surgery and have minimal side effects on intracranial pressure and postoperative recovery [1,2]. In this study, we aimed to examine intraoperative and postoperative patient data from several points of view; of anesthesia, postoperative morbidity and mortality, and the length of hospital stay; using the hospital records of the patients operated for intracranial mass in the period from 2008 to 2015 in Ankara Numune Training and Research Hospital.

The aim of this study was to perform a retrospective review of the intracranial mass cases in our hospital and to investigate the effects of anesthesia management on these patients.

Material and Methods

Study Universe and Sample Selection

The study universe of this study comprised the patients who were given general anesthesia for intracranial mass surgery in the Anesthesiology and Reanimation Clinic of Ankara Numune Training and Research Hospital. To establish the sample, the target was to gain access to the records of patients who were operated under general anesthesia from 2008 to 2015.

Type of Study

This is a retrospective observational study.

Inclusion and Exclusion Criteria

The study included 400 patients older than 18 years who were operated in the Department of Neurosurgery of our hospital for the treatment of intracranial mass under general anesthesia in the period from 2008 to 2015.

Data Sources and Study Conduct

The study started after obtaining approval from the Ethics Committee of the Ankara Numune Training and Research Hospital. The study data were collected reviewing the patient charts, files, and patient records in the electronic archives of the Anesthesiology and Reanimation Clinic of Ankara Numune Training and Research Hospital. Data of a total of 400 patients aged over 18 years, who had undergone intracranial mass surgery in the period from 2008 to 2015 were reviewed and collected. The patient files were retrospectively reviewed for collecting information about the following variables including age, gender, systemic diseases other than the cause of operation, type and location of the operated mass, the presence and extent of the intracranial shift in the preoperative period, the medications and doses used for induction and maintenance of anesthesia, all medications administered in the perioperative period, the intravenously administered fluids during the surgery and their types, blood products used intraoperatively, the amount of intraoperative bleeding, intraoperative urine output, intraoperative complications, intraoperative and postoperative levels of blood pressure and pulse, preoperative and postoperative laboratory test results, intraoperative end-tidal co2 values, postoperative nausea and vomiting, perioperative seizures, length of the operation, postoperative length of ICU stay, total length of hospital stay, and mortality.

Statistical Analyses

Descriptive statistical methods (frequency, mean, median, minimum, maximum, standard deviation) were used to evaluate the study data. The independent samples t-test was used for evaluating the quantitative data conforming to normal distribution. The Mann-Whitney U test was used, to test the quantitative data not conforming to normal distribution. The Chi-square and the Fisher's Exact tests were used for evaluating differences in the categorical data between the groups. SPSS Version 20 was used for obtaining statistical test results. $P<0.05$ was accepted as the statistical significance level.

Results

A review of the patient records in our hospital showed the data of 400 patients, who were older than 18 years and who were operated in our hospital for an intracranial mass. Of the study patients, 206 (51.5%) were women and 194 (48.5%) were men. The youngest patient was 18 years old and the oldest was 75 years old. The mean age of the patients in the study was 49.9 ± 12.9 years. When the average age is examined by gender, the mean age was 50.2 ± 13.9 years in women and 49.6 ± 11.9 years in men. There were no significant differences in gender by age ($p> 0.05$). Review of the comorbidities diagnosed preoperatively in the study patients revealed that 109 (27.3%) patients had essential hypertension, 65 (16%) patients had diabetes mellitus, 67 (16.8%) patients had chronic obstructive pulmonary disease, 9 (2.2%) patients had asthma, and 5 (1.2%) patients had goiter. No additional comorbidity was observed in 145 (36.2%) patients (Table 1). Of the study patients, 324 (81%) were ASA II, 72 (18%) were ASA III, and 4 patients (1%) were ASA IV (Table 1).

When tumor types of the patients were examined, it was observed that 124 (31%) patients had astrocytoma, 108 (27%) patients had meningioma, 56 (14%) patients had glioblastoma multiforme (GBM), and 24 (6%) patients had oligodendroglioma. Metastatic brain tumors were detected in 28 (7%) patients and benign lesions were found in 14 (3.5%) patients.

According to the localization of brain tumors in patients, supratentorial tumors were detected in 339 (84.8%) patients and infratentorial tumors were found in 61 (15.3%) patients. A review of the preoperative intracranial imaging studies showed that 39 (9.8%) patients had no cerebral shifts and 361 (90.2%) patients were identified with a cerebral shift. The mean shift distance was 4.39 ± 2.8 mm in all patients.

When anesthesia administered to the 400 study patients were reviewed, it was found out that all patients were operated under general anesthesia. For the general anesthesia induction, thiopental sodium was used in 251 (62.8%) patients, propofol was used in 147 (36.8%) patients, and etomidate was used in 2 (0.5%) patients. Of the 147 patients receiving propofol, 12 developed postoperative epileptic seizures; whereas, 24 out of 251 patients receiving thiopental sodium developed postoperative epileptic attacks. The frequency of postoperative epileptic attacks was not different between the propofol or thiopental sodium groups ($p = 0.811$). No statistically significant relationships were found between these two drugs used in

Table 1. General characteristics of the study population

	Total (n = 400)
Gender (Women/Men) (n) (%)	206 (51.5%) / 194 (48.5%)
Age (years)	49.9 ± 12.9
Comorbidity, n (%)	
Essential hypertension	109 (27.3%)
Diabetes Mellitus	65 (16%)
Chronic obstructive pulmonary disease	67 (16.8%)
Asthma	9 (2.2%)
Goiter	5 (1.2%)
No	145 (36.2%)
ASA Classification	Total (n = 400)
ASA II (n) (%)	324 (81%)
ASA III (n) (%)	72 (18%)
ASA IV (n) (%)	4 (1%)

Table 2. Anesthetic agents used in the study population

General Anesthetics Administered Intravenously for Induction	
Thiopental sodium (n) (%)	251 (62.8%)
Propofol (n) (%)	147 (36.8%)
Etomidate (n) (%)	2 (0.5%)
Inhalation Anesthetics Used For Maintenance	
Sevoflurane (n) (%)	393 (98.3%)
Desflurane (n) (%)	7 (1.8%)
Other Anesthetic Agents Adjunctive To Inhalation Anesthetics	
Nitrogen (n) (%)	341 (85.3%)
Remifentanil (n) (%)	59 (14.8%)

Table 3. Monitoring of intraoperative fluid replacement and blood products

Crystalloid and Colloids	
Physiologic Saline Solution (ml)	3376.6 ± 1996.6
Isolyte-S (ml)	881.9 ± 313.6
Ringer's Lactate (ml)	613.6 ± 342.7
Hydroxyethyl starch (ml)	742.2 ± 468.4
Total Fluid (ml)	4140.1 ± 2044.4
Intraoperative Fluid Loss	
Urine (ml)	769.3 ± 356.4
Bleeding (ml)	442.2 ± 358.4
Erythrocyte Suspension (n) (mean)	146 (628.8 ± 305.8 ml)
Fresh Frozen Plasma (n) (mean)	47 (330.3 ± 161.5 ml)
Values are given as mean ± standard deviation.	

induction and mortality (p = 0.148). When opioids were used in induction, mean 73.35 ± 33.1 mcg fentanyl was used and no fentanyl was used in 18 patients. A review of the anesthesia maintenance data showed that inhalation anesthesia was given to all study patients. Sevoflurane was used in 393 (98.3%) patients and desflurane was used in 7 (1.8%) patients. As adjuvants to inhaled anesthetic agents for the maintenance of anesthesia, nitrogen was used in 341 (85.3%) patients and intravenous remifentanil infusion was used in 59 (14.8%) patients. Additional use of intraoperative fentanyl at a mean dose of 44.6 ± 38.3 mcg was observed in 271 patients. Thiopental sodium was administered to 81 patients intraoperatively as an adjunct to anesthesia maintenance upon the request from the neurosurgery department. While 78 of these patients received 500 mg thiopental sodium, 3 received thiopental sodium at a dose of 250 mg. It was determined that vecuronium was used as a muscle relaxant in 263 (65.7%) patients and rocuronium was used in 137 (34.2%) patients (Table 2).

There were no statistically significant differences in the hemodynamic values anesthesia periods and intraoperative end-tidal CO2 pressure analyses.

It was found that a mean dose of 135.5 ± 68.2 mg mannitol was used in 355 patients during the operation. Mannitol was not used at all in 45 patients. The frequency of postoperative epileptic attacks was 1.1% in patients, who were not administered mannitol; while it was 1.5% in patients receiving mannitol. A statistically significant difference was not found in the frequency of epileptic attacks between the two groups (p = 0.494). The mortality rate was 2.3% in the patients, who did not receive mannitol; whereas it was 4.2% in patients, who received mannitol. There was not a statistically significant difference in the mortality rates between the two groups (p = 0.598).

The mean length of the operations was 281.2 ± 71.2 minutes.

Review of the intraoperative fluid management administered to the patients revealed that the mean volume of administered fluids was 4140.1 ± 2044.4 ml in total generally, the mean volume of saline solution was 3376.6 ± 1996.6 ml, the mean volume of isolyte-S solution was 881.9 ± 313.6 ml, the mean volume of ringer lactate solution was 613.6 ± 342.7 ml, and the mean volume of intraoperative hydroxyethyl starch was 742.2 ± 468.4 ml. The mean intraoperative urine output was 769.3 ± 356.4 ml (Table 3).

The mean volume of intraoperative bleeding calculated by the anesthetist was 442.2 ± 358.4 ml. Erythrocyte suspension was used in 146 of 400 patients and fresh frozen plasma was used in 47 patients. In the patients who received these blood products only, a mean volume of 628.8 ± 305.8 ml erythrocyte suspension and 330.3 ± 161.5 ml of fresh frozen plasma was used.

Of the study patients, 160 (40%) needed ephedrine and 83 (20.8%) needed nitroglycerin administration in varying doses intraoperatively.

Air embolism developed in 7 (1.8%) of the 400 patients in the study. Intraoperative mortality was not observed in any of these patients.

Of the antiemetic therapy administered by the anesthetist in the postoperative period, 35 (8.8%) patients received no antiemetics, 72 (18%) received metoclopramide, and 293 (73.3%) received ondansetron. Vomiting was observed in 105 (26.3%) patients. Compared to the group of individuals, who received no antiemetics but metoclopramide; the frequency of vomiting was significantly lower in the patients receiving ondansetron (n = 244, 61%) (p = 0.000).

Examination of the dose-vomiting relationship showed that vomiting occurred in 19 (13.2%) out of 144 patients receiving 4 mg ondansetron, in 12 (13.3%) of the 90 patients receiving 6 mg ondansetron, and in 18 (30.5%) of the 59 patients receiving 8 mg ondansetron.

There was a statistically significant difference among these three groups (p = 0.008).

For postoperative pain management, it was observed that

intravenous tramadol and metamizole sodium were used mostly. It was observed that tramadol alone was used in 170 (42.5%) patients, metamizole sodium alone was used in 100 (25%) patients, and a combination of both tramadol and metamizole sodium was used in 130 (32.5%) patients.

When the relationship between the tramadol use and vomiting was examined, vomiting was observed in 69 (23.0%) of 300 patients who received tramadol and in 36 (36.0%) of 100 patients who did not receive any tramadol. A statistically significant difference in vomiting between the two groups was revealed (p = 0.013) in the intergroup comparisons.

Epileptic attacks were detected in 36 (9%) patients during the postoperative period in the hospital. Investigation of the correlation between anesthesia management and the development of postoperative epileptic attacks revealed that there were no differences in the use of propofol or thiopental sodium for anesthesia induction (p = 0.46). The use of adjunctive thiopental sodium in the intraoperative period did not reduce the frequency of epileptic attacks (p = 0.089).

The mean length of stay in the postoperative intensive care unit stay was 5.9 ± 4.8 (min: 0, max: 52) days in the postoperative period and the mean length of hospital stay was 12.1 ± 5.0 (min: 3, max: 52) days.

Of the 400 patients included in the study, 15 (3.8%) died in the postoperative period. There was a significant relationship between the postoperative mortality and preoperative cerebral shift, with the mortality rate increasing as the extent of the shift increased (p = 0.001). There was not a statistically significant correlation between the postoperative epileptic attacks and mortality (p = 0.137). Investigation of the relationship between tumor location and mortality showed that there was no significant difference between infratentorial (mortality rate: 0.94%) or supratentorial tumors (mortality rate: 2.94%) in affecting the mortality rates (p = 0.62).

The evaluation of the vital signs measured in the postoperative neurosurgery intensive care unit revealed that the mean values were generally within normal limits.

Of the 400 study patients, 69 (17.3%) required positive inotropes and 80 (20%) required the administration of nitroglycerine postoperatively. The mortality rate in the 69 patients receiving positive inotropes was 17.4% while it was 0.9% in the patients, who did not receive these medications. The mortality rate was 80% in the 80 patients who received nitroglycerin postoperatively and it was found to be 3.4% in the 320 patients, who did not use this medication. There was no correlation between postoperative nitroglycerine use and mortality (p = 0.55) but mortality was high in the patients requiring the administration of positive inotropes in the postoperative period (p = 0.001).

Correlation analyses showed that the longer the duration of stay in the intensive care unit is associated with a higher rate of mortality (p = 0.000).

Examination of the relationship between the tumor types and mortality demonstrated no statistically significant differences (p > 0.05).

The results of the laboratory tests of the study; although there was a statistically significant difference between the preoperative and postoperative measurements of blood chlorine, potassium, urea, aspartate aminotransferase, and alanine aminotransferase levels, the results of these parameters were within the normal limits in both periods (p >0.05). It was observed that the mean values of the parameters, which were not statistically significant, were generally within the normal limits, too.

Discussion

Our study retrospectively examined the data, anesthesia approaches, and outcomes of 400 patients, who underwent a cranial mass excision surgery under general anesthesia in our hospital from the year 2008 to 2015. Our study results demonstrated that medications used in anesthesia induction for intracranial surgery was not different from each other in increasing postoperative seizure frequency and mortality. Secondly, we found a significant relationship between the extent of the preoperative cerebral shift with mortality rates. Thirdly, there was no difference in the frequency of postoperative seizures or mortality rates between the patients receiving mannitol or not in the intraoperative period. We observed that ondansetron was a more effective antiemetic agent when used intraoperatively.

The anesthesia practice in brain surgery differs in many ways from other methods employed in other types of surgical procedures. The critical issue in neuroanesthesia is to maintain the optimum cerebral perfusion in the intraoperative period to prevent postoperative complications. Therefore, the neuroanesthetists take a major part both in the intraoperative and postoperative period. Intraoperative monitoring methods essential for neuroanesthesia should be practiced and the follow-up should be precisely performed; an optimally selected group of anesthetics should be used according to the patient characteristics, intraoperative neuroprotective strategies should be developed, the patient stress should be alleviated with the administration of analgesic and antiemetic drugs postoperatively, and efforts should be spent to prevent seizures as much as possible. We examined the neuroanesthesia practices of our clinic in intracranial mass operations from the point of view presented above.

Approximately 40-45% of primary brain tumors during the first 15 years of life and 50-60% of brain tumors in adults originate from astrocytes. There are significant differences between adults and children in the reported incidences of these tumors when they are classified by specific histological types. Compared to other tumor types, astrocytoma and medulloblastomas are more frequent in the pediatric age group, whereas glial tumors and meningiomas are significantly more common in adulthood [3].

In our retrospective study, the most common tumor type in adult patients was astrocytoma at a rate of 31%, followed by a 27% rate of meningioma, a 14% rate of glioblastoma multiforme, and oligodendroglioma at a rate of 6%. Metastatic brain tumors were identified in 7% of the patients and benign lesions were observed in 3.5% of the patients.

The age distribution of central nervous system tumors peaks in childhood. Increasing frequencies are observed from the twenties to the age of 70, starting to decrease after this time point in the life span. A slight male dominance is observed in all

age groups [3].

However, according to our study, 51.5% of the patients who were operated for intracranial masses were women and 48.5% were men, with a mean age of 49.9 years in all patients. Although the incidence of brain tumors was slightly higher in women than in men, there were no differences in other types of epidemiological data in our study compared to the reports in the literature.

A review of the frequency of use of the anesthetic agents in neurosurgery reveals the common use of volatile anesthetics in the maintenance of anesthesia.

However, these agents have both favorable and unfavorable effects on the neurophysiological condition and being aware of these potential effects is critical both for the patient's wellbeing and performing a successful surgical procedure [4].

In our retrospective study, we observed that 393 patients received sevoflurane (98.3%) and 7 (1.8%) patients received desflurane for the maintenance of anesthesia. In addition, we found that nitro protoxide was used in 341 (85.3%) patients and intravenous remifentanil infusion was administered to 59 (14.7) patients. When we examined the patient files, we could not find any rationale for desflurane use.

Propofol reduces the cerebral blood flow, cerebral oxygen consumption, and intracranial pressure at induction doses. In addition to these properties, it changes the mean arterial pressure minimally when administered by titration. Furthermore, the major rationale for selecting this agent is the rapid recovery of the patient after its use [5].

Thiopental has been used in neuroanesthesia practice for nearly 70 years. The reduction of cerebral oxygen consumption and cerebral blood flow are the most important characteristic effects of this molecule; however, its half-life of up to 11-14 hours complicates the postoperative neurological evaluation. Although cerebral protective effects of thiopental is prominent, hypotension and reductions in stroke volume that may potentially occur after anesthesia induction may present a serious danger for patients undergoing neurosurgical procedures [6].

Selection of anesthetics for neuroanesthesia requires the anesthetist to consider the effects of medications on intracranial pressure, cerebral blood flow, and cerebral oxygen consumption. Thiopental is an ideal agent for neuroanesthesia because it reduces the cerebral blood flow rate and oxygen consumption, preventing cerebral ischemia and herniation. Furthermore, new drugs, including etomidate and propofol, with comparable brain-protective effects and other positive effects have been introduced to the use of anesthetists recently. The neuroprotective effects of these three abovementioned medications have been established besides their potential adverse effects. Knowing these untoward effects and the medical and surgical history of the patient allows us to select the optimum medication in special cases [8].

In a study by Ravussin et al., the hemodynamic parameters of the patients who used thiopental and isoflurane in one group or propofol in the other group were compared. The study included 60 patients, having otherwise no health issues. Half of the patients received thiopental for induction and isoflurane for the maintenance of anesthesia. In the remaining half of the study patients, propofol was used for both induction and maintenance of anesthesia. Both groups received 50% nitrous oxide and 50% oxygen. The result demonstrated that the changes in the heart rate, mean arterial pressure, and cerebral perfusion pressure were similar in both groups [7].

In our study, it was found that thiopental was used in 62.8% of patients and propofol was used in 36.8% of the patients. We considered that thiopental has been used almost as a gold standard in neuroanesthesia for a long time and the rates of thiopental use in our study reflect this perception. Furthermore, it has been demonstrated that thiopental is the drug with the lowest cost-effectiveness compared to propofol and etomidate; and this could be another reason for using this medication at high rates [7].

One of the most commonly used adjuvants in neuroanesthesia is mannitol. Mannitol is widely used for the treatment of increased intracranial pressure. Mannitol increases the osmolarity of the plasma, theoretically preventing water leakage from the intravascular compartment. Thereby, it reduces edema, viscosity of the blood viscosity, and hematocrit concentration, and improves microcirculation by direct vasodilatation effects. Mannitol improves the local cerebral blood circulation via these effects. Furthermore, mannitol shows ischemic edema-reducing effects and hydrophilic free radical scavenging activity. Besides its osmotic effects, mannitol reduces the synthesis of CSF, increases the cerebral blood flow rate and cerebral O2nd consumption, and reduces blood viscosity by improving perfusion. Therefore, the effects of mannitol in intracranial surgery are potentially useful [8].

H. Baran et al. demonstrated in their animal experiment that mannitol reduced epileptic attacks, prevented the reductions of noradrenaline levels in the amygdala and piriform cortex, and corrected behavioral changes in rats, which were injected kainic acid, a potent neuroexitator drug [8].

In a 27-patient study, Haglund et al. found out that furosemide and mannitol inhibited spontaneous epileptic activity and epileptiform activities induced by electrical stimulation; however, they reported no changes in normal EEG [9].

The requirement for randomized controlled trials investigating the use of mannitol in intracranial hypertension has been reported in the literature. However, international associations such as the European Consortium for Brain Injury recommend the use of mannitol to treat intracranial hypertension at an evidence level of two and three.

Although it is the most commonly used osmotic diuretic in the management of intracranial hypertension, there is insufficient evidence to determine the optimal dose of mannitol and duration of treatment [10].

According to the available information, infusion of 0.25-1 g/kg mannitol in 20-30 minutes is recommended. The use of higher doses is associated with serious side effects. Repeated doses have been reported to be associated with less efficacy and neurological complications due to increased osmolarity, including osmotic demyelination. Therefore, repeated doses of mannitol should be administered only if the osmolarity levels are monitored [10].

In our clinic, mannitol was frequently used in intracranial surgery cases. We did not find any significant differences in the incidence of postoperative seizures and mortality rates

between the patient groups receiving or not receiving mannitol treatment. We believed that the absence of statistically significant differences in the incidence of postoperative seizures and mortality rates between the mannitol-treated and non-mannitol-treated patients could have resulted from the different indications of mannitol use, the variable size of the masses, and the presence of brain edema.

Sudden changes in intravascular volume in neurosurgery cases are commonly seen due to hemorrhage, frequent use of potent diuretics, and diabetes insipidus. Therefore, fluid replacement therapy in neurosurgical cases requires anesthesiologists to select the type of fluid based on the following four factors, which include the effects of the type of fluid on developing brain edema, cerebral perfusion, serum glucose concentrations, and sodium homeostasis [11].

Administration of volatile anesthetics and potent vasodilators during the surgery may reduce the cardiac filling pressure despite the absence of significant changes in the intravascular volume. In such a case, the anesthesiologist should minimize the extent of the increase in the intracranial pressure and cerebral water content. Intracranial hypertension secondary to cerebral edema is currently the most common cause of intraoperative and postoperative morbidity and mortality. Hypotonic fluids should be avoided in the presence of neurological injury. Infusion of 5% dextrose or Ringer's lactate solution, and especially the administration of high doses, should be avoided because the Ringer's lactate solution contains 3 mEq/L calcium, which can cause reperfusion damage. In patients with head trauma, infusion of 0.9% NaCl is the right choice, as it is slightly hypertonic compared to plasma [11].

A review of the intraoperative fluid management in our study demonstrated that the most preferred type of therapy was the administration of physiologic saline crystalloids. Although there was a statistically significant difference in the preoperative and postoperative levels of blood sodium, potassium, calcium, and chlorine, all values in both periods were within normal limits.

Maintaining normal perioperative hemodynamics in neuroanesthesia is an important factor in maintaining cerebral perfusion pressure. Mean arterial pressure is directly related to the intracranial pressure and cerebral perfusion pressure. Arterial hypertension after craniotomy has been reported as one of the most common complications [12,13]. Acute postoperative arterial hypertension may lead to an increase in the intracranial pressure, causing cerebral hyperemia and vasogenic edema resulting in intracranial hemorrhage. Intracranial hemorrhage alone is a pathology that causes prolonged hospitalization and fatal complications [13]. Studies suggest preemptive prevention of hypertension because of its relationship with early postoperative bleeding. Maintenance of balanced anesthesia intraoperatively with the use of inhalational agents or with the combination of intravenous anesthetics and opioids is suggested to ensure the hemodynamic stability of the patients during awakening. Preemptive administration of beta-blockers and calcium channel blockers was recommended for this purpose. Esmolol is frequently recommended in the treatment of intraoperative acute hypertension because it does not have a cerebral vasodilatation effect [14].

Examination of the patient data on hemodynamic and vasoactive agents used in our study led to the observation that out of the 400 study patients, 69 (17.3%) required the administration of positive inotropic agents postoperatively and we found that mortality rate was significantly higher in these patients. Eighty (20%) patients with acute hypertension were treated with postoperative administration of nitroglycerine. We did not find a significant difference in mortality between the nitroglycerine-treated and non-treated groups of patients. Although nitroglycerin is not considered the first drug of choice for the treatment of hypertension, easy accessibility and economic advantages still constitute the major reasons for selecting this medication for use [15]. The fact that there was no esmolol available in our hospital during the study period was also another factor, leading us to this conclusion.

Intraoperative and early postoperative seizures are the most common pathologies after craniotomy. Seizure severity ranges from simple partial seizures to generalized seizures. The incidence of intraoperative seizures has been reported to be in the range from 0 to 36% [16].

In general, intraoperative seizures are self-limiting partial seizures and generalized seizures are rarely seen. However, epileptic attacks may cause inhibition of the spontaneous respiration in awake patients or in the postoperative period, potentially causing hypoxia and associated complications. Seizures are usually seen in the early postoperative period (first week after surgery) and especially in the first 6 to 24 hours. Identifying the risk factors and determination of seizure prevention strategies in the management of anesthesia may reduce seizure-related mortality and morbidity. In their study on craniotomy patients, Conte et al. observed seizures in one-third of the patients intraoperatively in their craniotomy cases and in 11% of the patients postoperatively [17]. We retrospectively examined 400 patients and observed that seizures occurred in 36 (9%) patients in the postoperative period. This incidence was in alignment with the study results of the patient series reported by Conte et al.

Conte et al. carries out a study on 316 patients with supratentorial craniotomies and determined the specific variables, increasing the risk of perioperative epileptic attacks [17]. These risk factors included young age, tumors location in the frontal and parietal lobes, pathological levels of arterial CO2, and general anesthesia. There are studies showing that low doses of propofol infusion may lead to increased electrocorticogram activity [18]. However, because of the positive effects mentioned above, this medication continues to be used in neuroanesthesia [18]. Our study results demonstrated that thiopental sodium was used in 251 (62.8%), propofol was used in 147 (36.8%), and etomidate was used in 2 (0.5%) patients. Postoperative seizures were observed in 12 out of 147 patients who received propofol, while postoperative seizures were observed in 24 out of 251 patients receiving thiopental sodium. The frequency of postoperative seizures did not show a statistically significant difference between the patient groups receiving either propofol or thiopental sodium. No statistically significant relationships were found between these two drugs used in induction in causing mortality ($p = 0.148$). When the relationship between the occurrence of postoperative seizures and anesthesia management was examined, no differences

were found between the use of propofol or thiopental sodium in anesthesia induction. The use of adjunctive thiopental sodium in the intraoperative period did not decrease the frequency of seizures. The studies in the literature report the surgical risk factors as the most common cause of epileptic attacks including the manipulation of the brain tissue and hematomas, but no significant differences were found among the types of surgical approaches [19].

Although we did not find a statistically significant relationship between the emergence of postoperative seizures and mortality in our study, the lack of long-term data on this issue is a limitation.

The relationship of the extent of cerebral shift with the mortality and morbidity has been investigated after the introduction of neuroanatomic imaging methods allowing for the identification of this pathology. Although pineal shift has been used as a diagnostic marker since 1924, the relationship between the extent of the shift and prognosis has been used since the 90s. In addition to the extent of the cerebral shift, which is included in the evaluation criteria, it is also important to determine whether it results from acute bleeding or a chronic lesion like a tumor. In general, a distance of a shift below 5 mm is benign and larger shifts are associated with higher mortality and morbidity [20].

Bartek et al. conducted a study on 979 patients in three centers and investigated various variables in terms of whether they could predict serious complications in intracranial meningioma surgery. They reported that serious complications were more common over the age of 70, in functionally dependent patients (Karnofsky performance scale score of <70), in patients undergoing operations longer than 4 hours, in the presence of severe comorbidities, and in men. In this study, tumor location, previous meningioma surgery, and brain edema were not found statistically significant in predicting serious complications [21]. However, Brell et al. conducted a study about craniotomy in brain tumors in 200 patients with gliomas and metastases. They found that the presence of an infratentorial mass, previous cranial radiotherapy, the dimensions of the surgical site and the presence of a midline shift of more than 10 mm increased the incidence of major complications [22].

Of the 400 patients included in the study, 15 (3.8%) died in the postoperative period. When the relationship between postoperative mortality and the extent of preoperative cerebral shift was examined statistically, it was found that there was a significant relationship between them and the mortality increased with the increased extent of the shift. However, in order to establish a relationship between the mortality and the presence of a shift, there is a need for conducting large-scale studies and meta-analyzes.

Postoperative nausea and vomiting is a very common morbidity in craniotomy procedures. Although various drugs are used in treatment, it still has a high incidence. This finding is thought to be caused by the surgical procedure and the intracranial mass regardless of the anesthesia technique administered. Latz et al. found a 47% incidence of postoperative nausea and vomiting in the first 24 hours and gave intraoperative antiemetics to 11% of these patients. Latz et al. found out that female gender and not using intraoperative steroids were additional risk factors. Anesthesia technique or the presence of infratentorial or supratentorial mass did not affect the incidence of nausea and vomiting [23].

A review of patient data about the intraoperative antiemetic treatments in our study showed that antiemetics were not used in 35 (8.8%) patients, metoclopramide was used in 72 (18%) patients, and ondansetron was used in 293 (73.3%) patients. When we investigated the incidence of vomiting in the postoperative period, we found that vomiting developed in 105 (26.3%) patients. When we compared patients using metoclopramide with ondansetron using patients, we found significantly low rates of vomiting in the latter group. Examination of the dose-vomiting relationship showed that vomiting occurred in 19 (13.2%) out of 144 patients receiving 4 mg ondansetron, in 12 (13.3%) of the 90 patients receiving 6 mg ondansetron, and in 18 (30.5%) of the 59 patients receiving 8 mg ondansetron. The differences among these three groups were statistically significant. Based on these results, we thought that factors including the location of the surgical site and increase in intracranial pressure were more effective in inducing vomiting rather than the ondansetron dose.

Pain occurring after craniotomy is considered to be low in intensity and is generally ignored. However, contrary to this assumption, moderate or severe pain is commonly reported after craniotomy and it is reported that the level of pain can be quite high especially within the first 2 hours following craniotomy. Local anesthetic injections, nonsteroidal anti-inflammatory agents, ketamine, opioids, and tramadol are used for pain relief. However, the search for an ideal analgesic agent continues for the treatment of patients suffering from severe pain after a craniotomy. The most important determining factor here is the patient's level of consciousness. If the patient is conscious and the patient perceives pain, postoperative analgesia should be performed [24]. Although the location of the craniotomy and the cause of the operation were reported to play a role in the severity of the pain, no differences were found between supratentorial and infratentorial tumors in inducing postoperative pain [25].

It is a fact that pain developing after craniotomy is insufficiently treated. For preventing the potential craniotomy pain, anesthetic agents not causing excessive sedation, increased pCO2 levels, and medications not affecting the intracranial pressure should be preferred. A multimodal approach including the infiltration of a local anesthetic, use of a non-steroidal anti-inflammatory agent, and administration of morphine or tramadol, may control or reduce this pain. We observed that tramadol and methimazole sodium were frequently used as intraoperative analgesics in our patients. We could not compare the efficacy of these analgesics because we could not obtain sufficient data from the review of patients' files.

Conclusion

The patients who were operated for intracranial mass were examined preoperatively, perioperatively, and postoperatively. The frequency of postoperative seizures did not change in association with the type of medications used for anesthesia induction. Intraoperative mannitol use did not have a significant effect on the occurrence of postoperative seizures and mortality.

We found that as the extent of preoperative cerebral shift

increased, the mortality rates increased. There were no significant changes in the hemodynamic parameters in the intraoperative period based on the type of anesthetic agents used in induction.

We think that ondansetron used for postoperative vomiting prophylaxis may have more preemptive antiemetic effects compared to metoclopramide. We observed higher mortality in patients requiring postoperative support with positive inotropes.

The current role of anesthesiologists has already passed beyond the line of ensuring the safety of the patient only during the operation but they aim to make critical contributions in the postoperative period as well. This is most commonly observed in brain surgery. It is predicted that the length of hospital stay and mortality rates can be positively affected with essential interventions, affecting early recovery in the postoperative period, preventing seizures, and controlling postoperative pain, nausea, and vomiting.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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